REMARKS

Claims 1-3, 9-17, 19-22, 28-36, 38-42, 47-55, 57-60, 66-74, 76-79, 85-93 and 95 are pending in the application. Claims 11-14, 30-33, 49-52, 68-71, 87-90 are withdrawn as drawn to processes that use the antibodies of the invention. Applicants respectfully request that these claims be rejoined to the invention upon finding the elected claims allowable and examined in this application. Claim 42 is canceled in the present amendment as drawn to a nucleic acid. Claims 1, 9, 10, 13-17, 19, 20, 28, 29, 32-36, 38, 39, 47, 48, 51-58, 66, 67, 71-74, 76-79, 85, 86, 90, 93 and 95 have been amended. By these amendments, Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

Applicants note that the pending claims listed by the Examiner include claims 77-79, 85, 86, 91-93 and 95, yet the Examiner acknowledges only the election of Group I and claims 77 and 91. Office Action at page 2. Applicants note that claims 77-79, 85, 86, 91-93 and 95 are in Group VII, which Applicants asserted should be included in Group I. Response filed May 27, 2005 at page 4. Applicants respectfully request that the Examiner clarify whether the claims of Group VII other than claims 77 and 91 are considered part of the elected invention.

The specification is objected to for containing embedded hyperlinks. Applicants have amended six paragraphs of the specification to remove hyperlinks.

Claims 1-3, 9, 10, 15-17, 19-22, 28, 29, 34-36, 38-41, 47, 48, 53-55, 57-60, 66, 67, 72-74, 76-79, 91-93 and 95 are objected to for allegedly reciting non-elected subject matter. Claims 1, 9, 15, 16, 20, 28, 34, 35, 39, 47, 53, 54, 57, 58, 66, 72 and 73 have been amended to recite only SEQ ID NO: 4 and SEQ ID NO: 2, the elected species. These amendments are made without prejudice. Applicants reserve the right to file divisional applications claiming the subject matter relating to SEQ ID NO: 3 and SEQ ID NO: 1.

I. Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-3, 10, 15, 19-22, 29, 34, 38-41, 47-48, 57-60, 66-67, 72-74, 76, 85, 86, 91-93 and 95 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to point out and distinctly claim the subject matter which the Applicant

regards as the invention. Office Action at page 3. The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). Applicants respectfully traverse.

A. Claims 1-3, 19, 20-22, 38-41, 57-60, 76-79 and 95 are rejected under 35 U.S.C. § 112, second paragraph for being indefinite because they recite "At least one isolated mammalian anti-Dengue virus antibody" in the preamble. Allegedly, the scope of the claim is unclear. Office Action at page 3. Claims 1, 19, 20, 38, 39, 57, 58, 76, 77 and 95, and dependent claims 2, 3, 21, 22, 40, 41, 59, 60, 78 and 79 have been amended to recite "An" instead of "At least one", as suggested by the Examiner.

B. Claims 10, 29, 48, 67 and 86 are rejected under 35 U.S.C. § 112, second paragraph for being indefinite because they recite "the effective amount of at least one compound or protein". Allegedly, the scope of the claim is unclear because it is allegedly unclear what the compound or protein is effective for. Office Action at page 3. Claims 10, 29, 38, 48, 67 and 86 have been amended to recite "a therapeutically or prophylactically effective amount". Support for this amendment is found in paragraph [0015] of the specification. These amendments introduce no new matter.

C. Claims 15, 29, 34, 48, 53, 67, 72 and 86 are rejected under 35 U.S.C. § 112, second paragraph for being indefinite because they recite improper Markush groups. Office Action at page 3. Claims 10, 13, 14, 15, 17, 29, 32, 33, 34, 36, 48, 51, 52, 53, 55, 67, 70, 71, 72, 74, 86, 89, 90 and 93 have been amended to correct the recitation of Markush groups.

D. Claims 19, 38, 57 and 95 are rejected under 35 U.S.C. § 112, second paragraph as being dependent on canceled claims. Office Action at page 3. Claims 19, 38, 57 and 95 have been amended to incorporate the language of the canceled claims from which they depended. Support for these amendments is in the claims as filed. These amendments introduce no new matter.

E. Claims 58-60, 66, 67, 72-74, and 76 are rejected under 35 U.S.C. § 112, second paragraph as being allegedly unclear in the recitation "the antibody binds to the same region of a Dengue virus protein as an antibody comprising at least one light chain CDR having the amino acid sequence of at least SEQ ID NO: 4." Allegedly it is unclear what protein or

epitope of the Dengue Virus is bound by the antibody comprising at least one light chain CDR having the amino acid sequence of at least SEQ ID NO: 4. Office Action at page 4. Applicants respectfully traverse.

The Examiner has not made a *prima facie* case that one of ordinary skill in the art would not understand what is claimed in claims 58-60, 66, 67, 72-74, and 76. It would be clear to one of skill in the art in light of the specification the meaning of the recitation "the antibody binds to the same region of a Dengue virus protein as an antibody comprising at least one light chain CDR having the amino acid sequence of at least SEQ ID NO: 4." The protein or epitope bound by the claimed antibody is "same region of a Dengue virus protein as [binds] an antibody comprising at least one light chain CDR having the amino acid sequence of at least SEQ ID NO: 4". The Examiner is apparently requesting that narrowing details describing the exact protein and exact epitope be put into these claims; however, breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). Applicants respectfully request reconsideration and withdrawal of the present rejection.

F. Claims 77-79 and 91-93 are rejected under 35 U.S.C. § 112, second paragraph as being allegedly unclear in the recitation "[a]t least one isolated mammalian anti-Dengue virus antibody, comprising at least one human CDR, wherein said antibody specifically binds to at least one epitope comprising at least 1-3 amino acids, to the entire amino acid sequence of a Dengue virus NS protein." Allegedly it is unclear how an epitope can be comprised of one amino acid. Office Action at page 4. Applicants respectfully traverse.

The Examiner has not made a *prima facie* case that one of ordinary skill in the art would not understand what is claimed in claims 77-79 and 91-93. The claim is clear in its description of "at least one epitope comprising at least 1-3 amino acids" and the Examiner has not explained how this is unclear. The Examiner's questioning of how an epitope can be comprised of one amino acid is not relevant to clarity of the recitation of an "epitope comprising at least 1-3 amino acids". Applicants respectfully request reconsideration and withdrawal of the present rejection.

Accordingly, Applicants respectfully request that these rejections of claims 1-3, 10, 15, 19-22, 29, 34, 38-41, 47-48, 57-60, 66-67, 72-74, 76, 85, 86, 91-93 and 95 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

II. Rejections under 35 U.S.C. § 102(b)

Claims 77-79, 85-86, 91-93 and 95 are rejected under 35 U.S.C. § 102(b) as being anticipated by Valdes *et al.* (*Clinical and Diagnostic Laboratory Immunology*, 2000, 7(5):856-857, "Valdes"). Office Action at page 4. Applicants respectfully traverse.

In order to support an anticipation rejection under 35 U.S.C. § 102, the Examiner must illustrate that each and every element of a claimed invention was disclosed within a single prior art reference. *In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990). A claimed invention is anticipated only when it is "known to the art in the detail of the claim." *Karsten Manufacturing Corp. v. Cleveland Golf Co.*, 242 F.3d 1376, 1383 (Fed. Cir. 2001). In other words, not only must the limitations of claim be shown in a single prior art reference, the limitations must be "arranged as in the claim." *Id.* Further, "to establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

Valdes does not disclose each and every element of the invention claimed in claims 91-93. Valdes does not disclose a "medical device" or a "delivery device or system" which uses one of the modes recited in the claim 93 comprising the anti-Dengue virus antibody. The Examiner asserts in an apparent inherency argument that Valdes performs a Western blot analysis by the "classical method" in which antibodies "are placed into a syringe with which the diluted solution containing the antibodies is injected into the electrophoresis gel sandwiched between glass plates prior to running the current through the gels." Office Action at pages 5-6. Respectfully, this is not how a "classical" Western blot analysis is performed. Rather, in a "classical" Western procedure, the protein antigens are loaded into an electrophoresis gel and the antibodies are used as probes in solution. *See*, Joseph Sambrook and David W. Russell, *Molecular Cloning, A Laboratory Manual* A9.28 (3rd ed. 2001), attached. Accordingly, one of skill in the art would not find that the use of a "medical device" or "delivery system or device" such as a syringe comprising anti-Dengue virus antibodies is "necessarily present" in Valdez.

Claims 77, 85 and 95 and their depending claims 78, 79 and 86 have been amended to recite "an isolated population of monoclonal mammalian anti-Dengue virus antibodies" or "a population of monoclonal mammalian anti-Dengue virus antibodies." These amendments are made without prejudice to or disclaimer of the subject matter thereof. Valdes does not teach or disclose a population of monoclonal anti-Dengue virus antibodies.

Accordingly, Applicants respectfully request that any rejections of claims 77-79, 85-86, 91-93 and 95 under 35 U.S.C. § 102(b) over Valdes be reconsidered and withdrawn.

CONCLUSION

Applicants have properly and fully addressed each of the Examiner's grounds for rejection. Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully submitted,

March 31, 2006

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Attachment

Joseph Sambrook and David W. Russell,
Molecular Cloning, A Laboratory Manual A9.28 (3rd ed. 2001)

Western Blotting

Western blotting (Towbin et al. 1979; Burnette 1981; Towbin and Gordon 1984) is to proteins what Southern blotting is to DNA. In both techniques, electrophoretically separated components are transferred from a gel to a solid support and probed with reagents that are specific for particular sequences of amino acids (western blotting) or nucleotides (Southern hybridization). In the case of proteins, the probes usually are antibodies that react specifically with antigenic epitopes displayed by the target protein attached to the solid support. Western blotting is therefore extremely useful for the identification and quantitation of specific proteins in complex mixtures of proteins that are not radiolabeled. The technique is almost as sensitive as standard solid-phase radioimmunoassays and, unlike immunoprecipitation, does not require that the target protein be radiolabeled. Furthermore, because electrophoretic separation of proteins is almost always carried out under denaturing conditions, any problems of solubilization, aggregation, and coprecipitation of the target protein with adventitious proteins are eliminated.

The critical difference between Southern and western blotting lies in the nature of the probes. Whereas nucleic acid probes hybridize with a specificity and rate that can be predicted by simple equations, antibodies behave in a much more idiosyncratic manner. As discussed earlier, an individual immunoglobulin may preferentially recognize a particular conformation of its target epitope (e.g., denatured or native). Consequently, not all monoclonal antibodies are suitable for use as probes in western blots, where the target proteins are denatured. Polyclonal antisera, on the other hand, are undefined mixtures of individual immunoglobulins, whose specificity, affinity, and concentration are often unknown. It is therefore not possible to predict the efficiency with which a given polyclonal antiserum will detect different antigenic epitopes of an immobilized, denatured target protein.

Although there is an obvious danger in using undefined reagents to assay a target protein that may also be poorly characterized, most problems that arise with western blotting in practice can be solved by designing adequate controls. These include the use of (1) antibodies (i.e., preimmune sera, normal sera, or irrelevant monoclonal antibodies) that should not react with the target protein and (2) control preparations that either contain known amounts of target antigen or lack it altogether.

Often, there is little choice of immunological reagents for western blotting — it is simply necessary to work with whatever antibodies are at hand. However, if a choice is available, either a high-titer polyclonal antiserum or a mixture of monoclonal antibodies raised against the denatured protein should be used. Reliance on a single monoclonal antibody is hazardous because of the high frequency of spurious cross-reactions with irrelevant proteins. If, as is usually the case, monoclonal and polyclonal antibodies have been raised against native target protein, it will be necessary to verify that they react with epitopes that either (1) resist denaturation with SDS and reducing agents or (2) are created by such treatment. This test can be done by using denatured target antigen in a solid-phase radioimmunoassay or in western dot blots.

In western blotting, the samples to be assayed are solubilized with detergents and reducing agents, separated by SDS-polyacrylamide gel electrophoresis, and transferred to a solid support (usually a nitrocellulose or PVDF filter), which may then be stained (e.g., with Ponceau S). The filter is subsequently exposed to unlabeled antibodies specific for the target protein. Finally, the bound antibody is detected by one of several secondary immunological reagents (e.g., ^{125}I-labeled or anti-immunoglobulin, or anti-immunoglobulin or protein A coupled to horseradish peroxidase or alkaline phosphatase), followed by autoradiography, enhanced chemiluminescence, or enzymatic production of a colored precipitate. As little as 1–5 ng of an average-sized protein can be detected by western blotting. For more information on western blotting, please see Appendix 8.

Molecular Cloning

A LABORATORY MANUAL

THIRD EDITION

Front cover (paperback): The gene encoding green fluorescent protein was cloned from *Aequorea victoria*, a jellyfish found in abundance in Puget Sound, Washington State. This picture of a 50-mm medusa was taken on color film by flash photography and shows light reflected from various morphological features of the animal. The small bright roundish blobs in the photograph are symbiotic amphipods living on or in the medusa. The bright ragged area in the center is the jellyfish's mouth.

Bioluminescence from *Aequorea* is emitted only from the margins of the medusae and cannot be seen in this image. Bioluminescence of *Aequorea*, as in most species of jellyfish, does not look like a soft overall glow, but occurs only at the rim of the bell and, given the right viewing conditions, would appear as a string of nearly microscopic fusiform green lights. The primary luminescence produced by *Aequorea* is actually bluish in color and is emitted by the protein aequorin. In a living jellyfish, light is emitted via the coupled green fluorescent protein, which causes the luminescence to appear green to the observer.

The figure and legend were kindly provided by Claudia Mills of the University of Washington, Friday Harbor. For further information, please see Mills, C.E. 1999–2000. Bioluminescence of *Aequorea*, a hydromedusa. Electronic Internet document available at http://faculty.washington.edu/cemills/Aequorea.html. Published by the author, web page established June 1999, last updated 23 August 2000.

Back cover (paperback): A portion of a human cDNA array hybridized with a red fluor-tagged experimental sample and a green fluor-tagged reference sample. Please see Appendix 10 for details. (Image provided by Vivek Mittal and Michael Wigler, Cold Spring Harbor Laboratory.)

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